IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	David P. Katz	) Group Art Unit 1654
Appl. No.	:	10/001,684	)
Filed	:	October 25, 2001	)
For	:	METHODS AND COMPOSITIONS FOR THE BENEFIT OF THOSE SUFFERING FROM POLYCYSTIC OVARY SYNDROME WITH CHROMIUM COMPLEXES	)
Examiner	:	P. Patten	)

DECLARATION OF JAMES KOMOROWSKI UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, James Komorowski declare and state that:

1. I am the Vice President of Technical Services and Scientific Affairs at Nutrition 21, Inc., the assignee of the above-mentioned application. Our research at Nutrition 21, Inc. targets the diabetes marketplace and related health markets where poor insulin function is a metabolic risk factor. These markets include obesity, metabolic syndrome, cardiovascular disease, Polycystic Ovary Syndrome (PCOS), and depression.

2. I received a Bachelor of Arts degree in biology from State University of New York and a M.S. in medical biology from Long Island University.

3. I have extensive experience in investigating the role of chromium in ameliorating metabolic disorders including, among others, PCOS. Prior to serving as Vice President of Technical Services and Scientific Affairs, I was the Director of Product Development at Nutrition 21, Inc. from July 1999-2001 and Senior Manager, Clinical and Regulatory Affairs from July 1997 to July 1999. I spent nine years in the pharmaceutical industry, holding project management, clinical research, and regulatory affairs positions at major pharmaceutical companies. Additionally, I have worked for a number of years in

academia as a research associate at New York Hospital for Special Surgery and Memorial Sloan-Kettering Cancer Center.

4. Over my career, I have completed more than 100 research studies, submitted over 10 regulatory submissions to the FDA, and am an inventor on over 12 patents. I lead Nutrition 21, Inc.'s scientific research team. Our research efforts have begun to reveal the role of chromium in complex metabolic and biochemical pathways linking diabetes, cardiovascular health, obesity, depression, PCOS and other health conditions. We believe that insulin resistance may be the common denominator among these diseases.

5. I am familiar with the specification and claims of U.S. Patent Application Serial No. 10/001,684, the outstanding Office Action, and the prior art cited therein. I am also familiar with the NIH-funded pilot study performed by researchers at State University of New York (SUNY), Stony Brook.

6. PCOS is a little-understood hormonal condition that is the leading cause of infertility. At present, there is no FDA-approved drug specifically designed to treat PCOS. While some doctors prescribe insulin-sensitizing agents including metformin, these agents have been associated with undesirable side effects including nausea, diarrhea, and loss of appetite. While decreased insulin sensitivity is associated with PCOS, this is a complex, multifaceted disease. There is substantial uncertainty regarding its causes and treatments, and as such, it is not possible to predict with any level of confidence whether any particular agent, untested in this disease, would or would not have a beneficial effect. This was the case with chromium agents including chromium picolinate. While chromium is known to have a beneficial effect in facilitating insulin function, there was no way to know whether such facilitation would be realized in PCOS, or whether any such facilitation would have a beneficial effect on those suffering from the disease.

7. The National Institutes of Health (NIH) recognizes the significance of PCOS and the lack of any approved therapy. NIH also recognizes the need to develop effective treatments for this condition. Thus, NIH recently funded a pilot study to evaluate the efficacy of daily supplementation with 1,000 μg of chromium as chromium picolinate as a potential new nutritional therapy for women suffering from PCOS. In the study, researchers at the State University of New York, Stony Brook, analyzed the effects of nutritional supplementation with chromium on six women with PCOS. The results of the study showed that insulin sensitivity was significantly increased by an average of 35% after two months of treatment and baseline insulin levels decreased by 22%. These results were presented at the 59th Annual Meeting of the American Society for Reproductive Medicine Conference.

8. The study leader said, "If larger, controlled trials confirm chromium picolinate's efficacy, PCOS patients could potentially take the supplement every day to reduce their risk of diabetes and possibly improve other physical and symptomatic effects of PCOS." (See Exhibit B to accompanying Amendment and Response to Office Action.) The results of the study confirm that dietary supplementation with a chromium complex may

significantly reduce symptoms associated with PCOS, including insulin insensitivity, diabetes, and other physical and symptomatic effects of PCOS.

9. The resulting data from the pilot study are unexpected in light of the prior art. The potential role of chromium in PCOS apparently was not obvious to NIH, which funded a study to develop such data. To the best of my knowledge, our researcher at Nutrition 21, Inc. was the first to discover the amelioration of symptoms of PCOS following chromium supplementation. The surprising results discussed and claimed in the specification of U.S. Patent Application Serial No. 10/001,648 were confirmed by an independent research group at State University of New York. I am not aware of any previous publication that conclusively reports significant reduction in symptoms associated with PCOS using chromium. The de la Harpe et al. reference merely discloses the use of chromium in lowering serum glucose levels, lowering serum lipid levels, and increasing lean body mass. The Ostlund et al. reference describes the use of a carbohydrate, pinitol, for treating insulin resistance. These references, though, have little or no predictive value in ascertaining whether chromium would have therapeutic value in PCOS. Indeed, the pharmaceutical sciences are notoriously unpredictable, and the biological systems affected by a disease such as PCOS are often complex and intertwined.

10. The data provided by the NIH-funded pilot study confirms the present patent disclosure: it shows that chromium supplementation significantly reduces symptoms of PCOS and therefore offers promise to those individuals suffering from PCOS.

11. The resulting data described above and in the attached press release (Exhibit B) were unpredictable given the teachings of the prior art and the understanding in the field prior to the present invention. While one can, in hindsight, partially explain the results in terms of chromium facilitating insulin function, it is nevertheless true that efficacy was unpredictable prior to conducting the appropriate tests.

12. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: March 01, 2004 James Komorowski

James Komorowski, M.S.

Health and Nutrition

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New NIH-Funded Pilot Study Indicates CP Supplementation May be an Effective Treatment for PCOS
10/15/2003

New NIH-Funded Pilot Study Indicates Chromium Picolinate Supplementation May be an Effective Treatment for Polycystic Ovarian Syndrome (PCOS)

Promising Nutritional Therapy for 2 Million American Women

Presented at American Society for Reproductive Medicine Conference (ASRM)

San Antonio, TX, October 15, 2003 (Nutrition 21, Inc., Nasdaq: NXXI) -- Results of a new pilot study funded by the National Institutes of Health (NIH) showed that daily supplementation with 1,000 mcg of chromium as chromium picolinate significantly enhanced insulin sensitivity. These initial results offer a potential new nutritional therapy for approximately 2 million American women suffering from Polycystic Ovarian Syndrome (PCOS). PCOS is a little-understood hormonal condition that is a leading cause of infertility, and is associated with insulin resistance, gestational diabetes and type 2 diabetes. The study was presented at the 59th Annual Meeting of the American Society for Reproductive Medicine Conference (ASRM) in San Antonio, Texas and appears in a supplement to *Fertility and Sterility*, September 2003.

In an effort to build on limited PCOS treatment options, researchers at the State University of New York (SUNY), Stony Brook, analyzed the effects of nutritional supplementation with chromium in the form of Chromax® chromium picolinate on six women with PCOS. Results showed that glucose disposal rate (insulin sensitivity) was significantly increased by an average of 35% after two months of treatment, and baseline insulin levels decreased by 22%.

"Chromium picolinate, which has positive effects on insulin sensitivity in people with type 2 diabetes, looks like it has great potential as a safe, effective

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long-term therapy to fill a void in treating PCOS," said Michael L. Lydic, MD, assistant professor at SUNY Reproductive Endocrinology Division, who led the study. "If larger, controlled trials confirm chromium picolinate's efficacy, PCOS patients could potentially take the supplement every day to decrease their risk of diabetes and possibly improve other physical and symptomatic effects of PCOS. It also has potential to be used in combination with prescription insulin-sensitizing drugs."
Today there is no FDA-approved drug specifically to treat PCOS. Some doctors prescribe insulin-sensitizing agents, such as metformin. However, many women experience unwanted side effects such as nausea, diarrhea, and loss of appetite, making ongoing treatment for insulin resistance prohibitive. Dr. Lydic added, "Our goal is to explore potential long-term therapies to bring insulin resistance under control and decrease risk of diabetes. Ideally, we hope to compare chromium picolinate with metformin in a clinical setting."

"An emerging body of research continues to confirm the findings that chromium insufficiency is an important nutritional factor in insulin resistance which is strongly associated with the type 2 diabetes epidemic," said Gail Montgomery, President and CEO. "It is rewarding to see that Chromax supplementation shows promise as an affordable, convenient therapeutic option for women suffering from PCOS."

Clinical Design
The study was a non-randomized, prospective study, which included six women of reproductive age (18 –42 years old) with PCOS and signs of insulin resistance. Hyperinsulinemic, euglycemic clamp tests, the most accurate measure of insulin sensitivity, were used on all subjects.

Researchers measured hormonal, physical and symptomatic effects of improved insulin function. They reported that one subject without menstrual cycles, who had the largest change in glucose disposal rate, had a spontaneous menstrual period after 2 months. No adverse side effects were reported among the study participants.

The study was funded by NIH grant No. M01RR10710, and product was supplied by Nutrition 21, Inc.

About Chromium

Chromium is an essential mineral that is needed for insulin activity in carbohydrate, fat and protein metabolism. Numerous clinical trials have shown that chromium as chromium picolinate reduces insulin resistance, improves blood sugar control and may help reduce the risk of cardiovascular disease and type 2 diabetes.

About Nutrition 21

Nutrition 21 is an industry leader in using pharmaceutical quality research to substantiate the health benefits of nutritional supplements. It holds 24 patents for chromium compounds and their uses, and 11 other nutrition patents. The Company's proprietary technologies focus on chromium picolinate and its relationship to insulin resistance, a condition implicated in type 2 diabetes, cardiovascular disease, obesity and depression. Nutrition 21 markets Chromax® chromium picolinate, the leading chromium ingredient used in supplements. The Company is developing its first branded product, Diachrome™, for people with type 2 diabetes intended to be marketed through healthcare channels. More information is available at www.nutrition21.com, www.chromax.com, www.diachrome.com.

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Editors Note: The study cited above was conducted and presented independently. Nutrition 21 distributed this press release, with the review and approval of the researchers.